

selves, the newer cephalosporins vary in activity against individual bacteria and in pharmacokinetics.

Cefotaxime, moxalactam and cefoperazone are the only third-generation cephalosporins licensed in the United States but others, such as ceftazidime, should soon follow.

Most third-generation cephalosporins have excellent activity in vitro against strains of *Escherichia coli*, *Klebsiella*, *Proteus*, *Providencia*, *Morganella* and *Citrobacter*. Normal peak serum concentrations of these drugs exceed by 100 times the minimal inhibitory concentration of the microorganisms. Third-generation cephalosporins also have excellent activity against the  $\beta$ -lactamase-producing strains of *Haemophilus* and *Neisseria* species and against anaerobes. Activity against *Pseudomonas aeruginosa* varies; their value depends on comparative testing with extended-spectrum penicillins and aminoglycosides. Activity against *Staphylococcus aureus* is significantly less than that of cefazolin and, because activity against *Streptococcus pyogenes* and *Streptococcus pneumoniae* is also less than the penicillins, the third-generation cephalosporins offer no advantage in treatment against these Gram-positive species. These drugs have no activity against group D streptococci (enterococci) and *Listeria*.

Adverse side effects are infrequent and are similar to those with other cephalosporins: namely, rash, diarrhea, *Candida* vaginitis, instances of granulocytopenia and thrombocytopenia and transient elevations in hepatic enzyme levels. Prolongation of the prothrombin time, which is correctable with vitamin K administration, has been observed with moxalactam. Superinfection with multiresistant organisms is a potentially important complication as these drugs may promote the prevalence of resistant bacteria.

In clinical trials the third-generation cephalosporins have been effective in treating respiratory tract, urinary tract, abdominal and gynecologic infections and meningitis due to Gram-negative enteric bacteria. However, except for cases of Gram-negative meningitis, in which treatment with moxalactam or cefotaxime has dramatically increased the success rate, clinical studies comparing third-generation cephalosporins with conventional antimicrobial therapy have shown only equivalence. These remarkable and expensive new drugs thus provide an additional means of therapy of potential but unproved superiority to present regimens.

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## Periodic Health Examinations

PERIODIC HEALTH EXAMINATIONS are an American institution. Their earliest roots can be traced to successful public health programs aimed at controlling such diseases as typhoid, tuberculosis and smallpox. The basic principles that stimulated the growth and acceptance of this movement are simple and seductive: that peri-

odic examinations can detect diseases in asymptomatic persons in an early stage and that prompt treatment will lead to diminished morbidity and mortality. Early uncontrolled studies showed impressive health gains. The American Medical Association formally endorsed the annual examination in 1922 and prepared a manual detailing the methods of providing this service. Over the next 50 years, comprehensive periodic health examinations became the standard of care and a symbol of the best in American medicine. While epidemiologists identified risk factors for such major health problems as coronary artery disease, early detection programs for cervical, colon and breast cancer showed promising results and biomedical engineers provided automated multiphasic testing. Increasing public demands fostered by a profitable health industry led to the use of more and more untested screening procedures.

In spite of this popular support, critics of routine periodic screening have recently begun to question the purpose, content, frequency, yield and cost of such examinations. At the same time, government and other third-party insurers and health maintenance organizations are insisting on closer evaluation of efficacy and cost effectiveness of many health care practices. Results of a number of ambitious studies of periodic health screening have recently been published. Although each reaches somewhat different conclusions, they are similar in their attempt to place the periodic health examination on a sound, scientific foundation.

The most comprehensive of these studies was published in 1979 by the Canadian Task Force on the Periodic Health Examination. An expert, 11-member panel supported by an international group of consultants spent more than three years reviewing the world medical literature on 78 potentially preventable conditions. To ascertain whether early detection would be beneficial, available information on the burden of suffering, the characteristics of the early detection procedure and the effectiveness of preventive measures or treatment modalities was carefully evaluated. The task force incorporated their conclusions into a lifetime program of 18 health protection packages. For example, at specified intervals for all adults, measurement of blood pressure, examination of oral cavity, evaluation of hearing, stool screening for occult blood, immunization against tetanus, counseling against smoking and alcoholism and advocacy of the use of seat belts were recommended. For adult women, periodic contraceptive counseling, physician breast examination and a Papanicolaou's test were added. Yearly mammography was suggested for women between 50 and 60. For adults older than 65 years, periodic assessment of physical, social and psychologic function and yearly influenza immunization were recommended. The task force failed to find sufficient evidence to justify routinely doing a "complete" history and physical, blood count, chemistries, analysis of urine, electrocardiography and chest x-ray.

It should be emphasized that the recommendations of the task force and those of the other three recent

studies are for preventive measures on behalf of apparently well, asymptomatic persons at low medical risk. They are not intended for those persons at increased risk of a condition or who have symptoms. There remains a great deal to be learned about the efficacy of periodic health examinations. Well-designed studies to assess the usefulness of health screening procedures still remain to be done. Accepting that many of these recommendations are based on incomplete data, primary care practitioners should select a periodic screening measure consistent with their interpretation of available information and incorporate it into a specific plan of preventive care for each patient.

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## Acquired Immune Deficiency Syndrome (AIDS)

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS) is the term currently applied to an expanding epidemic of severe immunosuppression first recognized as an increased occurrence of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia among previously healthy persons. Between June 1, 1981, and February 10, 1983, the Centers for Disease Control (CDC) received reports of 1,051 cases of acquired immune deficiency syndrome (that is, Kaposi's sarcoma or serious opportunistic infections) with fatality in 41 percent overall and in greater than 60 percent in those diagnosed more than a year ago. Although 80 percent of the reported cases were concentrated in six cities, predominantly on the East and West Coasts, well-documented cases have occurred in more than 33 states and 13 foreign countries. The reported incidence continues to rise rapidly.

Populations considered to be at risk include homosexual or bisexual men (75 percent of cases), heterosexual male and female intravenous drug abusers (13 percent), heterosexual Haitians with no history of in-

travenous drug abuse (6 percent) and persons with hemophilia A (three cases). Although the CDC's definition of acquired immune deficiency syndrome requires the unexplained occurrence of Kaposi's sarcoma, *P carinii* pneumonia or infections associated with defective cell-mediated immunity, the full spectrum of the syndrome may include asymptomatic abnormality of lymphocytes now reported in gay men and nonspecific constitutional symptoms with or without generalized lymphadenopathy. The prevalence of other malignant disorders (diffuse undifferentiated non-Hodgkin's lymphoma, squamous carcinoma of the anorectum and of the oral cavity) and autoimmune thrombocytopenia also appears to be increased in gay men.

The pathogenesis of acquired immune deficiency syndrome is unknown. Epidemiologic evidence is most consistent with the presence of an agent or agents transmissible by blood. Two immunosuppressive and oncogenic herpesviruses, cytomegalovirus and Epstein-Barr virus, are candidate agents, but genetic (HLA-DR5) factors and amyl nitrite exposure have also been implicated.

There is no laboratory screening test for acquired immune deficiency syndrome. Immunologic abnormalities in established cases have included lymphopenia, cutaneous anergy and alterations in T-lymphocyte subsets as measured by monoclonal antibodies to markers for suppressor and helper function. However, delayed cutaneous hypersensitivity and quantitatively normal lymphocyte counts do not exclude a significant defect in immunoregulation and abnormalities in T-cell subsets are not yet established as predictive of the development of this disorder.

Physicians should be familiar with the features of this syndrome and keep patients in identified risk groups under surveillance. Gay men who wish to reduce their risk should reduce the number of sexual partners.

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